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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,470	07/21/2003	Debbi Drane	017227-0190	4517

22428 7590 09/29/2006

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,470	DRANE ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 44-99* is/are pending in the application.

4a) Of the above claim(s) *56-62,77-83 and 86-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,44-55,63-76 and 84-85* is/are rejected.

7)☒ Claim(s) *1 and 64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 44-99 are pending.

Response to the Amendment

This is to acknowledge the amendment filed on July 13, 2006. Claims 1 and 64 have been amendment. Claims 56-62, 77-83, 86-99 were withdrawn from the consideration. Claims 1, 44-55, 63-76 and 84-85 are considered before the examiner.

Claim Rejections - 35 USC § 112 withdrawn

1. the rejection of claims 64-76, 84-85 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicants' amendment.

Claim Rejections - 35 USC § 102

2. Claims 1, 46, 47, 48, 49-55, 64, 67-76, 85 are still rejected under 35 U.S.C. 102(b) as being anticipated by Garcon et al. WO 98/15287A1 on the same ground stated in the previous office action.

3. In response to the previous office action, applicants amend claims 1 and 64 and submit that the compositions of Garcon et al. in WO 98/15287A1 requires alum and the method for making the immunogenic composition according to the teachings of Garcon et al. was first adsorbed to alum before the addition of MPL or QS21, thus, the antigen was adsorbed to an inorganic carrier before an organic carrier was even introduced, indicating that there was no direct electrostatic interaction between the organic carrier and antigen. Additionally, neither the MPL nor the QS21 taught by Garcon et al. in WO 98/15287A1 is an organic complex. Thus, Garcon et al. in WO 98/15287A1 lacks any teaching whatsoever of a negatively charged organic complex in electrostatic association with a charged antigen.

4. Applicants' argument has been fully considered' however, it is not found persuasive because the argument of different methods of making the claimed composition does not encompasses the claims. The claimed immunogenic composition still comprises the same components as those Garcon et al. teach in WO 98/15287A1 (see claims 1-8). The same immunogenic composition taught by Garcon et al. inherently posses all chemical and biochemical characteristics as well as immunological activity as the claimed immunogenic

complex. In fact, Garcon et al. teach that said adjuvant formulation elicits the enhanced Th2 and Th1-type immune responses represented by a high INF-λ, T-cell proliferation and CTL responses (see Figs. 1-7).

5. Moreover, there is no scientific basis indicating why the claimed saponin, sterol, and monophosphoryl lipid A are not the same saponin, sterol, and monophosphoryl lipid A taught by Garcon et al. in WO 98/15287A.

6. Applicants are reminded that Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products.

7. See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) [PTO can require an applicant to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical.] While "indirect comparisons, based on established scientific principles, can validly be applied to distinguish a claimed chemical process or product from that disclosed in the prior art,"

8. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 432 (CCPA 1977), the comparisons must be scientifically valid.

9. Patent owner's burden under the circumstances presented herein was described in In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows: Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on `inherency' under 35 U.S.C. § 102, on `prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted].

10. To this context, the rejection is maintained.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 44-55, 63-76, 84-85 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Garcon et al. WO 98/15287A1 and Coppoer et al. (Immunity, 1999, April, Vol. 10, pp. 439-449) and John et al. (Hepatology 1999, Vol. 30, No. 4, pp. 1037-1044).

13. In response office action, applicants amend claim and submit that the compositions taught by Garcon et al. is different from the claimed immunogenic composition because 1). they are made by different method. 2). Neither the MPL nor the QS21 taught by Garcon et al. is an organic complex. 3). There is no disclosure or teaching in Garcon et al. that would motivate a skilled artisan to make an immunogenic complex in which a negatively charged organic complex and a charged antigen are electrostatically associated. 4). Garcon et al. also lacks any evidence for the induction of CTLs, and only shows evidence of Thl responses. 5) Finally, although Garcon I disclosed HCV antigen, they do not teach how to choose antigen(s) and how to optimize a CTL response to antigen(s).

14. Applicants' argument has been fully considered' however, it is not found persuasive for the following reasons set forth below:

15. The claims are generally directed to an immunogenic complex comprising an HCV antigen with at least 10 amino acid residue as a T cell epitope and adjuvants including a saponin, and sterol, wherein the organic complex comprising saponin and a phospholipids, preferably a phosphoryl lipid A. However, this characteristic of an immunogenic complex has been generally taught by the Garcon et al. in WO 98/15287A1 (See claims 1-8) as discussed above. Moreover, the immunogenic composition taught by Garcon et al. is also able to elicit Th1-type immune responses, which is characterized by high INF-λ, T-cell proliferation and CTL responses (see Figs. 1-7), because these high INF-λ, T-cell proliferation and CTL responses are all belonged to the Th1 type immune response rather than Th2 type immune response, which is substantiated by Cruse et al. (Illustrated Dictionary of Immunology 2nd edition, published on 2003 by CRC, see pages 577-578). Therefore, the method for making the claims immunogenic complex differently

from the method taught by Garcon et al. does not change the claimed product having different structural and functional characteristics compared to the immunogenic composition taught by Garcon et al. (Claims 1-8).

16. Regarding the reference of Cooper et al. although Applicants admit that Cooper teaches a method for identifying HCV immunogenic epitopes that are able to induce a strong CTL immune response against HCV antigen," Applicants still assert that Cooper does not disclose an immunogenic composition, but merely suggests that certain HCV antigens might be important in vaccines, based on an examination of which HCV antigens induced CTL responses in 'cured' chimps. Chimpanzees, however, may not respond to HCV in the same manner as humans. Accordingly, a demonstration that CTLs in chimps react with specific epitopes is not a teaching or suggestion that the same epitopes are relevant in humans.

17. Applicants' argument that the reference fails to show certain features of applicants' invention is not found persuasive, because theses features (i.e., CTL epitope specified for human or a precise CTL epitope) are not recited in the rejected claim(s). Moreover, there is not any precise CTL epitope defined in the claims.

18. Regarding the reference by John et al. Applicants admit that John teaches several HCV core antigen epitopes being more reliable for inducing a T-cell mediated response against HCV infection, but applicants still argue that John actually lacks a disclosure of an immunogenic complexes for inducing a CTL response. In particular, John's teaching would not lead a skilled artisan to use the core or envelope antigens in an immunogenic complex in the present claims.

19. Applicants' argument against the John et al. is an argument against the references individually. To being with, there is no any particular core or E1 envelope antigen structure except at least 10 amino acid residues cited in the generically claimed HCV core and E1 antigens in the claims. The claims are generically directed to any at least 10 amino acid residues of HCV CTL epitope, John et al. teach several HCV T cell epitopes of Core antigen and E1 envelope antigen that all have at least 10 amino acids and are able to induce a significantly T cell mediated immune response for variants of different HCV strains (See entire document, especially, Table 2 and Fig. 4), which meets the limitations as claims drafted. More importantly, the disclosure by John's reference indicates that the HCV CLT epitopes had already been known in the art prior to the application was originally filed.

20. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

21. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

22. In this case, because the cited reference of Garcon et al. already teaches every element of the claimed immunological complex , which is also able to produce an enhanced Th1 immune response, the reference by Cooper et al, also teaches how to select and measure the activity of a HCV CTL epitope and the reference by John et al. even teaches precisely some CTL epitopes of HCV core and E1 antigens, in order to produced an enhanced Th1 type immune response, an ordinary skilled in the art would have been obvious to be motivated to use any HCV CTL disclosed by John et al. or select a HCV CTL epitope by the method taught by Cooper et al. for preparation of an immunogenic composition taught by Garcon et al.

23. As there is no unexpected result presented by the application, the claimed invention as a whole is still considered prima facie obvious absence unexpected results. The rejection is maintained.

Conclusion

No claims are allowed.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

25. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bao Qun Li
09/19/2006

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